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EXAMINER	
STEADMAN, DAVID J	
ART UNIT	PAPER NUMBER
1656	

NOTIFICATION DATE	DELIVERY MODE
11/20/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/076,416	RIEPING ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23,25-28,33 and 35-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,25-28,33 and 39-42* is/are rejected.

7)☒ Claim(s) *35-38* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 23, 25-28, 33, and 35-42 are pending in the application.

[2] Applicant's amendment to the specification, filed on 8/11/09, is acknowledged.

[3] Receipt of a terminal disclaimer, filed on 8/11/09, is acknowledged.

[4] Applicant's remarks filed on 8/11/09 in response to the non-final Office action mailed on 4/29/09, are acknowledged. Applicant's arguments have been fully considered and are deemed to be persuasive to overcome at least one of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[5] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

[6] The rejection of claims 23, 25-28, 33, and 39-42 under 35 U.S.C. 103(a) as being unpatentable over Farwick-1, Farwick-2, Farwick-3, Farwick-4, Farwick-5, Burke-1, Burke-2, Burke-3, Burke-4, Burke-5, Hans, Nampoothiri-1, Nampoothiri-2, Nampoothiri-3, Nampoothiri-4, Mockel-1, Mockel-2, Mockel-3, Dusch, Wehmeier, Dunican-1, Dunican-2, Dunican-3, Dunican-4, OR Dunican-5 in view of Kramer, Grabau, Chang-1, and Chang-2 is withdrawn in view of the instant specification amendment and applicant's statement at pp. 3-4 of the remarks, which disqualifies the cited references as prior art under 35 U.S.C. 103(c).

[7] The rejection of claims 23, 25-26, 28, 33, and 42 under 35 U.S.C. 103(a) as being unpatentable over Kikuchi (US Patent 5,932,453) in view of Shimizu (US Patent 5,445,948) and Chang (*J Bacteriol* 154:756-762, 1983; cited as reference V in the Form PTO-892 mailed on 10/19/05) is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action. See item [7] beginning at p. 3 of the Office action mailed on 4/29/09.

[8] The rejection of claim 27 under 35 U.S.C. 103(a) as being unpatentable over Kikuchi in view of Shimizu and Chang as applied to claims 23, 25-26, 28, 33, and 42 above and further in view of Matsui (US Patent 4,391,907) is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action. See item [8] beginning at p. 5 of the Office action mailed on 4/29/09.

[9] The rejection of claims 39-41 under 35 U.S.C. 103(a) as being unpatentable over Kikuchi in view of Shimizu and Chang as applied to claims 23, 25-26, 28, 33, and 42 above and further in view of Dunican (US Patent 6,586,214) is maintained for the reasons of record and the reasons set forth below. The rejection was fully explained in a prior Office action. See item [9] beginning at p. 6 of the Office action mailed on 4/29/09.

RESPONSE TO ARGUMENT: Beginning at p. 4 of the instant remarks, applicant addresses the reference of Shimizu, arguing that the examiner's assertion that Shimizu

teaches that acetate generally inhibits growth of *E. coli* in culture is not true. According to applicant, Shimizu teaches a concentration above 17 g/L of acetate inhibits the growth of *E. coli.*

Applicant's argument is not found persuasive. Initially it is noted that applicant addresses the references of Shimizu and Chang individually, where the rejection is based on a combination of references. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicant's remarks addressing Shimizu, although applicant asserts that Shimizu teaches a concentration above 17 g/L acetate inhibits *E. coli* growth, it is noted that Shimizu teaches that it is preferable to control the acetate concentration in a culture medium to "6 g/liter or less" (column 4, lines 44-50), where the results of Shimizu indicate that 6 g/L of acetate is achieved at 10 hours of culturing (column 4, lines 42-43). Thus, Shimizu prefers to maintain acetate concentration at 6 g/L or less in the culture medium.

The examiner acknowledges that a generalized statement was made with respect to the teachings of Shimizu. However, the examiner's statement regarding acetate inhibiting growth of *E. coli* was not intended to suggest that *any* concentration of acetate inhibits growth of *E. coli* in culture. This is clearly borne out by the noted teachings of Shimizu. The examiner's reliance on Shimizu is based on Shimizu's teachings that culturing of *E. coli* for production of a desired product results in

production of a growth inhibiting substance, *i.e.,* acetate, and that at a certain concentration achieved during routine culturing of 10 hours or more inhibits *E. coli* growth (column 4). Shimizu suggests removing the acetate from the culture medium to enhance production of a desired product by culturing the *E. coli* (column 6). It should be noted that the L-amino acid production methods of Kikuchi (column 10, lines 44-45) and Matsui (column 4, lines 64-65) each uses an *E. coli* culturing time of greater than 10 hours and thus the teachings of Shimizu are relevant to the production methods of Kikuchi and Matsui.

Addressing the reference of Chang, applicant argues that only with hindsight reasoning would one combine the reference of Chang with Shimizu. Applicant argues that Chang's inability to explain feeble growth of *E. coli* on acetate produced by pyruvate oxidase is an indication of the unpredictable effects of genetic modification. Applicant further argues that Chang does not use L-amino acid production strains and it cannot be concluded that similar results could be achieved using a production strain.

Applicant's argument is not found persuasive. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Chang's inability to explain feeble growth of *E. coli* on acetate produced by pyruvate oxidase (p. 762, column 1) is irrelevant with respect to whether or not one of ordinary skill in the art would have been motivated to combine Chang with Shimizu and the other cited references. Chang acknowledges that pyruvate oxidase (poxB, encoded by *poxB* gene) produces acetate (p. 756, column 1, top) and suggests production of acetate can be blocked by an *E. coli* strain with an inactivated *poxB* gene (p. 762, column 1, top). Shimizu teaches that acetate inhibits *E. coli* cell growth at a certain concentration during routine culturing. Thus, one would have been motivated to inactivate a *poxB* gene in the *E. coli* of Kikuchi or Matsui with a reasonable expectation of inactivating its corresponding catalytic activity that results in acetate production, motivated by a desire to reduce acetate in the culture medium. Although applicant asserts that one cannot conclude that similar results would have been achieved in an L-amino acid production strain of Kikuchi or Matsui, applicant provides no rationale or line of reasoning to support this allegation. To the contrary, since the method of Kikuchi or Matsui uses an *E. coli,* one of ordinary skill in the art would have had a reasonable expectation that inactivating the *poxB* gene in the *E. coli* of Kikuchi or Matsui would have had the effect of inactivating its corresponding catalytic activity.

Claim Rejections - Double Patenting

[10] The provisional obviousness-type double patenting rejection of claims 23, 25-28, 33, and 39-42 as being unpatentable over: 1) claim 44 of co-pending US non-

provisional application 10/794,417 and claim 33 of co-pending US non-provisional application 11/350,043 is withdrawn in view of the instant terminal disclaimer.

[11] The provisional obviousness-type double patenting rejection of claims 23, 25-28, 33, and 39-42 as being unpatentable over: 1) claim 22 of co-pending US non-provisional application 10/812,315 and 2) claim 40 of copending Application No. 11/658,477 is maintained for the reasons of record and the reasons set forth below. The provisional rejections were fully explained in a prior Office action. See the Office action mailed on 5/27/08 at pp. 7-9 and the Office action mailed on 4/29/09 at pp. 8-9.

RESPONSE TO ARGUMENT: At p. 6 of the instant remarks, applicant requests that the provisional rejections be withdrawn and permit the application to issue as a patent. This is not found persuasive since this provisional rejection is not the only remaining rejection in the application.

[12] Claim(s) 23, 25-28, 33, and 39-42 are newly rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 8 and 22 of US Patent 7,504,242; claims 7 and 19 of US Patent 6,759,218; and claim 4 of US Patent 7,205,131 OR are newly provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 27 of co-pending application 10/847,610 in view of Kramer (*J. Biotechnol.* 45:1-21, 1996; cited in the PTO-892 filed on 4/20/04), Grabau (*J. Bacteriol.* 160:1088-1092, 1984; cited in the 9/3/02 IDS), Chang et al. (*J Bacteriol* 154:756-762, 1983; cited in the PTO-892

filed on 10/19/05; "Chang1"), and Chang et al. (*J. Bacteriol.* 167:312-318, 1986; cited in the IDS filed on 9/3/02; "Chang2"). This rejection is necessitated by the instant specification amendment and applicant's statement to disqualify references as prior art, wherein applicant states that the above cited patents and published application 2004/0214219 (corresponding to application 10/847,610) are subject to a joint research agreement or share a common assignee.

The claim(s) of the patents and co-pending application are drawn to a method of L-amino acid production using a *C. glutamicum* bacterium with an attenuated poxB gene. The difference between the claim(s) of the patents and co-pending application and the claimed method is that the claim(s) of the patents and co-pending application use a *C. glutamicum* bacterium rather than an *E. coli* bacterium.

The reference of Kramer teaches that *C. glutamicum* and *E. coli* are the workhorses of industrial amino acid production. See particularly p. 1.

The reference of Grabau teaches cloning of an *E. coli* poxB gene (abstract).

Chang1 teaches an *E. coli* with an inactivated *poxB* gene by insertional mutagenesis and Chang2 teaches an *E. coli* expressing a PoxB polypeptide with a C-terminal deletion that substantially decreases PoxB activity.

Therefore, it would have been obvious to modify the methods of the '242, '218, and '131 patents or the method of the '610 co-pending application to practice a method of L-amino acid production using an *E. coli* with an inactivated *poxB* gene. One would have been motivated to do this because it is recognized in the prior art that *E. coli,* like *C. glutamicum,* is used in the industrial production of L-amino acids.

Conclusion

[13] Status of the claims:

Claims 23, 25-28, 33, and 35-42 are pending.

Claims 23, 25-28, 33, and 39-42 are rejected.

Claims 35-38 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

No claim is in condition for allowance.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/David J. Steadman/
Primary Examiner, Art Unit 1656